Summer Fellow	Fellow Trainee Level	Mentor	Project Title	Lay Summary
Appenzeller, Cailey	Undergraduate	Noelle Gillis	CRISPR Screening for Epigenetic Modulators That Enhance Thyromimetic GC-1 Efficacy in Anaplastic Thyroid Carcinoma Cells	Anaplastic thyroid carcinoma (ATC) is a rare and aggressive cancer that is hard to treat. Many patients don't improve with current therapies, including newer targeted drugs. This project will test a new approach using CRISPR, a tool that can turn specific genes on and off. We will use CRISPR to turn off genes in ATC cells called "epigenetic regulators" which control how other genes involved in cancer growth and drug resistance behave. At the same time, we will treat the cancer cells with a drug called GC-1, which past studies show slows thyroid cancer growth. By combining these approaches, we aim to discover which genes make ATC cells easier to kill with GC-1, and which genes help the cancer survive GC-1 treatment. Understanding these patterns will help doctors choose better treatment plans for their patients and lead to more effective therapies for this deadly cancer.
Bassi, Taylor	Undergraduate	Michael Brasino	Engineering a Split T7 RNA Polymerase Logic Gate in Lactobacillus for Non-Invasive Lung Cancer Screening	Lung cancer is the deadliest cancer worldwide, largely because it is rarely caught early enough to be treated effectively. Existing screening methods are expensive and inconvenient. The proposed project is part of a larger effort to develop a novel screening tool: a genetically modified probiotic bacterium, Lactobacillus, that can be safely inhaled and detect biomarkers of lung cancer, and in response release molecules detectable in urine. This project focuses on engineering bacteria to emit molecules only when they detect multiple different biomarkers simultaneously using a split T7 system. My previous work has confirmed that this split T7 system functions properly in E. coli. This summer's work will involve transferring the system into Lactobacillus, bringing this tool one step closer to clinical use.
Boisoneau, Jaime	Graduate	Frances Carr	Disruption of Thyroid Hormone Signaling by PFOS	Thyroid cancer incidence has been rising in recent years and environmental endocrine disrupting chemicals may play a role. PFOS is a man-made chemical used in nonstick and water-resistant products that can interfere with the body's hormone

				system. Normally, the thyroid hormone T3 binds to a nuclear thyroid hormone receptor (TR), which controls how cells function by activating or suppressing gene transcription. One specific type of receptor, TRβ, acts as a tumor suppressor by maintaining healthy cell behavior and preventing thyroid cancer formation. However, recent studies have shown that PFOS competes with endogenous ligand T3 for binding to TRs, thereby disrupting the thyroid's normal signaling mechanisms. This could cause cells to behave abnormally and become more susceptible to cancer initiating events. Our research studies how PFOS disrupts TRβ signaling pathways and whether it can push a healthy thyroid cell toward a disease-like state by changing gene activity and cell behavior.
Chyong, Donian	Medical	Diego A. Adrianzen Herrera, MD	Retrospective analysis of the effects of psychosocial determinants of health on outcomes following induction therapy for adults with acute myeloid leukemia treated in the University of Vermont Health Network from 2010-2019	For adults with acute myeloid leukemia (AML), demographic, psychiatric, social, economic, and immobility characteristics at diagnosis can be ascertained from electronic health records and used to calculate a risk score measuring psychosocial vulnerability. After accounting for AML-specific clinical and laboratory data, this score will be correlated with AML patients' response to therapy, determining the relative effects of each risk factor and the utility of the score in assessing a patient's psychosocial vulnerability. I am currently conducting a similar analysis in the Massachusetts General Hospital's adult AML population. This summer project conducted at UVM will allow a multi-site follow-up analysis and comparisons between urban and rural populations. The overall objective is to show how a psychosocial vulnerability risk score is associated with treatment outcomes in AML. If successful, I hope the score can help identify and alleviate an AML patient's highest risk barriers to accessing care.
Davis, Emily	Medical	Ashley Volaric	Global Molecular and Clinicopathologic Characterization of Angioimmunoblastic T-cell	Angioimmunoblastic T-cell lymphoma (AITL) is a rare type of blood cancer that is not very well understood. Because it is difficult to identify, most patients with AITL are diagnosed late and often do not survive for longer than 2 to 3 years. Several

			Lymphoma (AITL) in Rural Vermont	potential risk factors have been identified, but it is still not clear which of these factors are the most significant in determining whether someone develops cancer. This project focuses on connecting several of these risk factors to characteristics of patients in the rural Vermont population with a diagnosis of AITL. The hope is that, by better understanding who is at high-risk for development of these tumors, we can diagnose individuals earlier and improve their long-term outcomes.
Eller, Margaux	Medical	Rohit Singh	Effect of Timing of Induction Immunotherapy in Melanoma.	My summer research project examines whether the timing of immunotherapy (a type of treatment that boosts your immune system to fight cancer) administration affects treatment outcomes in melanoma patients at the UVM Cancer Center. Through a retrospective chart review, we will analyze whether patients receiving morning versus afternoon/evening immunotherapy experience differences in immune-related adverse events and survival rates. Based on established relationships between circadian rhythms and immune function, we hypothesize that morning administration will yield superior outcomes. This research aims to provide evidence that could guide future immunotherapy scheduling protocols to optimize both treatment efficacy and patient safety at the UVM Cancer Center.
Flaherty, Patrick	Medical	Jenna Winebaum	The Impact of Prior Antibiotic Exposure on Oncologic Outcomes Following Bacillus Calmette-Guérin Therapy for Non-Muscle Invasive Bladder Cancer: A Retrospective Cohort Study	Immunotherapies are treatments that utilize the immune system to kill cancer. There is evidence that antibiotic exposure before receiving immunotherapy is associated with earlier cancer relapse, progression, and death. This is thought to result from changes in the microbiome, the community of bacteria in our bodies, which may impact immune response. Bladder cancer is the 5th most common non-skin cancer in the US. Bacillus Calmette-Guérin (BCG) is a bacterium that is injected into the bladder in patients with non-muscle invasive bladder cancer (NMIBC). It activates immune cells to kill the cancer. In this study, we will analyze antibiotic exposure prior to BCG for NMIBC, to see if it is associated with earlier disease recurrence,

				progression, or death. If antibiotics are associated with worse oncologic outcomes, future studies could explore approaches of antibiotic stewardship or microbiome supporting therapies such as fecal microbiota transplantation as strategies to improve BCG efficacy.
Foster, Sky	Undergraduate	Seth Frietze	Defining BRPF1 as a Regulator of Estrogen Receptor–Dependent Chromatin Activation in Breast Cancer	This project studies a protein called BRPF1 and its role in estrogen receptor–positive (ER+) breast cancer, which makes up about 70% of cases. These cancers grow in response to estrogen, and while treatments that block estrogen are often effective, many tumors eventually become resistant. BRPF1 helps control how DNA is packaged inside cells, allowing certain genes to be turned on. Early findings suggest that removing BRPF1 reduces the ability of estrogen to activate genes that drive cancer growth. In this project, I will use a system that allows rapid removal of BRPF1 in breast cancer cells to examine how it affects gene activity and cell growth. I will also test whether targeting BRPF1 improves responses to existing therapies. This research aims to determine whether BRPF1 is essential for cancer cell survival and could serve as a new target for treating resistant breast cancer.
Harlan, Julia	Undergraduate	Michael Toth	Targeting adipose tissue wasting to attenuate tumor growth in a preclinical model of lung cancer	Lung cancer is an important focus of research at the UVM Cancer Center. Many people with lung cancer develop cancer cachexia (CC), a disorder that causes a loss of muscle and fat, especially in later stages of disease. CC can make people feel worse in daily life, make treatments less effective, and lead to more health problems and early death. Even though CC is common, there isn't a standard treatment for it because the way it develops is not well understood. In earlier studies, our lab showed that mice lose body fat very early during the onset of CC, which suggests that fat loss may help tumors grow.

				Because of this, we are studying whether a drug that stops fat loss can also slow tumor growth. Our goal is to find a treatment that can slow cancer growth while preserving muscle and fat mass in patients with CC.
Hurley, Alyssa	Graduate	Steven Roberts	Transcriptional Regulatory Mechanisms of APOBEC3A in Breast Cancer	Every cell in our body has its own copy of our DNA, which is like a cookbook full of recipes that our cells use to make proteins they need to function. I study a protein called APOBEC3A or A3A for short. A3A is supposed to help your cells fight off viruses by damaging viral DNA, preventing viruses from making their own recipes. However, A3A can't tell the difference between viral DNA and our DNA, which can lead to cancer if it damages our DNA. I'm trying to understand what causes breast cancer cells to make more A3A, by looking at the DNA "recipe" for A3A. Similarly to a cookbook, the recipes for our genes have instructions for cooking and may be bookmarked or have notes to speed up the recipe. These details may be the key to understanding why cancer cells make too much A3A.
Kennedy, Mac	Post-Baccalaureate	Vitor Mori	Estimating the solid tumor mechanical properties that drive drug retention following intratumoral injections through the Needle-Induced Cavitation technique.	Lung cancer, in both men and women, accounts for the greatest number of cancer related deaths worldwide. Many patients are treated with chemotherapy, which travels through the blood to reach tumors. However, these drugs can also destroy healthy cells and cause side effects that affect a patient's quality of life. One possible solution is to inject the drug directly into the tumor so that more of the drug reaches the cancer and less affects healthy tissues. Our research group has found that even when a drug is injected directly into a tumor, the amount that stays inside can vary significantly. Sometimes the drug leaks out or distributes unevenly. In this project, we will study how tumors behave when fluid is injected into them. By understanding how tumors behave mechanically under injections, we hope to improve how doctors

				deliver cancer drugs directly into tumors and potentially enhance the safety and efficacy.
Kratochvil, Leah	Medical	Oluwatosin Akintola	Patterns of pseudoprogression in glioblastoma and effects on survival	Pseudoprogression (PsP) in glioblastoma is defined by the Glioblastoma Foundation as "an appearance of tumor growth on brain scans post chemotherapy and radiation when there is no tumor growth." Since PsP mimics true tumor progression (TP) radiographically, efficacious treatment may be discontinued prematurely in the setting of suspected TP/actual PsP, or new treatment initiation may be delayed in the setting of suspected PsP/actual TP. PsP also has implications for quality of life (QOL), as it can present with mild to severe clinical features which may require additional treatment. Lastly, mechanisms underlying PsP may be markers of responsiveness to treatment. Thus, PsP in glioblastoma may influence progression-free survival (PFS) or overall survival (OS). We plan to conduct a retrospective cohort analysis to evaluate effects of PsP on PFS, OS, and QOL in glioblastoma patients as well as to identify clinical factors that modify this relationship in a multivariate analysis.
Lewisesquerre, Anders	Undergraduate	Sylvie Doublie	Structural and biochemical characterization of human DNA polymerase β variants implicated in error-prone DNA repair	DNA in every cell in the human body is constantly being damaged from exposure to the sun and chemicals that distort the DNA structure. The human body can fix this type of damage using DNA polymerase beta, a protein that replaces the damaged section of the DNA by filling it with the correct DNA sequence. This process is important for maintaining the stability of DNA and thus preventing diseases like cancer. My project studies how mutations in this protein impact its ability to repair DNA, potentially contributing to cancer development. By understanding how these mutations cause errors in DNA repair,

				we can better predict how they may affect a patient's response to cancer treatment.
McGuirl, Katherine	Undergraduate	Paula Deming	Investigating the effects of STK11 C-Terminal Domain mutations on the pro-metastatic behaviors of EMT and anoikis resistance in lung adenocarcinoma	Lung cancer is the leading cause of cancer-related death worldwide, and lung adenocarcinoma (LUAD) is its most common form. Many LUAD tumors carry mutations in the STK11 gene, a tumor suppressor that normally regulates cell growth and prevents cancer spread. Most loss-of-function STK11 mutations disable the protein's enzymatic activity, leading to aggressive tumors characterized by increased metastasis and therapy resistance. In previous work, we identified 28 previously unrecognized STK11 mutations from patient tumor samples. Three of these mutations caused the STK11 protein to accumulate in the cell nucleus rather than its normal location. Despite retaining enzymatic activity, cells expressing these variants showed increased migration and invasion, key steps in cancer metastasis. These findings suggest that some STK11 mutations may disrupt function by altering where the protein resides within the cell, despite maintaining enzyme activity. This project will test whether nuclear-localized STK11 variants promote tumor spread similarly to complete STK11 loss.
McTigue, Madeline	Graduate	Alan Howe	Investigating the role of PKA phosphorylation of tensin-3 in cell-matrix adhesions	The spread of cancer cells to new sites in the body, a phenomenon known as metastasis, is responsible for 90% of cancer related deaths. Metastasis requires dysregulation of the processes that govern a cell's attachments to its environment. A cell attaches to its environment through a subcellular structure called cell-matrix adhesions (CMAs) which, in addition to mediating cell attachment, are responsible for integrating signals from a cell's environment to regulate migration. While cell migration is an essential process in healthy cells, like wound healing, cancer cells co-opt this process to metastasize. My research focuses on understanding the subtle changes to CMAs that impact cell attachment and migration in healthy and cancer cell settings. Under the duration of this award, I will seek

				to understand how small changes to one CMA protein, tensin-3, impact how CMAs integrate signals, ultimately to uncover a novel mechanism of regulation in cell attachment and migration.
Medeiros, Stasha	Graduate	Elise Tarbi	Identifying Communication Factors Influencing Connection in Telehealth Serious Illness Conversations with Rural Cancer Patients, Caregivers, and Clinicians (TeleConnect-2.0)	Many factors shape communication interactions between patients and clinicians, including what is said, in what way, and in what setting. In this study, we explore how communication factors influence how rural-dwelling people with cancer develop a sense of connection with their clinician using telehealth for their cancer care. Traditional research approaches, like interviews, can highlight "good communication" strategies, but cannot tie those strategies back to patient experiences and health outcomes. Simulated communication experiments provide a research tool that can overcome these challenges. This study is part of a multi-phase study which seeks to build realistic communication scenarios for later testing in simulated environments. In our previous interviews with rural patients with cancer about their telehealth experience, we learned what communication factors matter to them; this study builds on these findings, using interviews with patients, caregivers, and clinicians to develop and get feedback on telehealth simulations for later experimental testing.
Mittelstadt, Isabelle	Graduate	Steven Roberts	Investigating the mutational landscape of UV-exposed tissue within the UVMCC catchment area	Melanoma is the most dangerous type of skin cancer, and in Vermont, we have one of the highest rates of melanoma occurrence in country. However, neighboring states in New England do not have comparably elevated melanoma rates, therefore, we are especially interested in figuring out why Vermonters are more likely to develop this type of skin cancer. Skin cancer happens when the DNA of cells is damaged by UV radiation and this damage is converted into mutations that cause cells to divide uncontrollably. For my project, I will be taking skin from patients with skin cancer, isolating and growing different types of cells, then sequencing the DNA. By looking at

				the number and type of UV-induced mutations, we hope to see unique patterns that help to explain why Vermonters get melanoma so often, and people in other states don't.
Moriarty, Haley	Graduate	Trishnee Bhurosy	A Survey of Healthcare Providers' Perspectives on Food Insecurity in Adolescent and Young Adult Cancer Survivors	This project aims to look at how food insecurity affects adolescent and young adult (AYA) cancer survivors (ages 15-39 at diagnosis) from the perspectives of the healthcare providers (e.g., oncologists, social workers, nurses) who work with them. We will survey these providers in rural areas such as Vermont, upstate New York, and Maine to identify screening practices and recommendations for improving overall nutrition security in AYAs and other groups of survivors. Young cancer survivors are at increased risk for food insecurity, especially in rural areas. Yet, there are limited resources available to target this issue. Findings from this project will be used to develop future interventions that can be integrated within oncology healthcare providers' workflows to improve food security.
Petersen, James	Undergraduate	Karen Glass	Structural and Functional Dissection of the PfBDP1 Ankyrin Repeat Domain as a Reader of Acetylated Histones	Epigenetics refers to processes that control when genes are turned on or off without changing the underlying DNA sequence. Disruptions in these processes are a major driver of cancer, and the proteins involved have become important targets for cancer therapies. In cells, DNA is wrapped around proteins called histones. Chemical modifications to histones can influence whether nearby genes are active or silent. One important modification is acetylation. Bromodomain proteins recognize acetylation and help activate gene expression. Recent work in our laboratory suggests that another domain within bromodomain proteins may bind acetylated histones more easily than the domain previously thought to be responsible for this interaction. This summer, I will study the

				structure and function of this newly identified domain to further our understanding of epigenetic regulation. This work may also provide insight into how epigenetic dysregulation contributes to cancer and help guide the development of novel therapies.
Price, Alexa	Graduate	Alan Howe	Unraveling the molecular determinants of PKA within cell-matrix adhesions	A cell's attachment to its surrounding environment is necessary for cell survival. Cells attach to their surroundings through structures called cell-matrix adhesions (CMAs). CMAs are complex structures made up of a diverse set of cellular components and are highly dynamic, which allow the cell to attach or move through our body at regulated times. In cancer, a tumor cell's ability to regulate this movement can be hijacked, causing the cancer to move to other parts of the body in a process called cancer metastasis. My research sets out to understand how the various components of CMAs interact with one another and influence cell behavior, ultimately to understand how these components contribute to the tumor microenvironment and cancer metastasis.
Sicat, Alexandra	Undergraduate	Seth Frietze	Chemical-Genetic Targeting of the Chromatin Regulator BRPF1 to Evaluate its Role in Anaplastic Thyroid Cancer Cell Proliferation	Anaplastic thyroid cancer (ATC) is an aggressive disease with limited treatment options, in which cancerous cells grow uncontrollably and begin to harm surrounding areas of the body. BRPF1 is a protein that helps to mediate the expression of genes in our DNA, and plays a role in cancer cell growth, though its exact function in ATC is not well understood. This project will utilize a research method in which scientists attach a special tag to the BRPF1 protein, so that when a specific chemical is added the cell breaks down and removes that protein. By measuring how fast thyroid cancer cells then grow or divide in the absence of the protein, researchers can see whether BRPF1 is important for cell proliferation and survival. These findings may identify BRPF1 as a therapeutic target, while also providing hands-on training in molecular biology and cancer research techniques.

Wagner, Ethan	Graduate	Jason Stumpff	Identifying Mitotic Mechanisms of Resistance to KIF18A Inhibition in Chromosomally Unstable Cancers	Cancer affects millions of people each year and is the second highest cause of death in the United States. Most current cancer treatments harm healthy cells along with cancer cells, causing side effects like weakness and hair loss. To improve this, treatments that specifically target cancer cells are needed. Our lab recently found that some cancers depend on a protein called KIF18A for survival. When KIF18A is inhibited, cancer cells die with little impact on healthy cells, making KIF18A an intriguing target for therapy. However, some cancer cells adapt and survive without this protein, becoming resistant to KIF18A inhibitors. To understand how this happens, we will investigate the molecular basis of inhibitor resistance. By identifying molecules that take over KIF18A's job, we will elucidate how resistance is facilitated and how KIF18A inhibition can be improved as a cancer treatment.
Way, Regan	Undergraduate	Michael Brasino	Bacterial RNA Detection System for Lung Cancer	The human body is made up of tiny building blocks called cells. Each cell contains information in the form of DNA and RNA that tells it what to do. Sometimes a change, called a mutation, is made to the DNA that makes the cells multiply uncontrollably, which causes cancer. We are working to find a way to use healthy bacteria to detect lung cancer by identifying a mutation in the RNA that is pushed outside of the cell. When the bacteria encounter these strands of RNA, they will produce a different molecule that can be more easily detected by scientists. Right now, complicated tests are needed to screen for lung cancer, so it is usually not caught until the cancer has taken over. Using bacteria to detect cancer would make it easier to find it earlier, so it would be easier to treat.